

What is Claimed is:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

(a) a first nucleotide sequence which is a polymorphic variant of a reference sequence for Interleukin 4 Receptor Alpha (IL4R $\alpha$ ) gene or a fragment thereof, wherein the reference sequence comprises SEQ ID NO:1, and the polymorphic variant comprises an IL4R $\alpha$  isogene defined by a haplotype selected from the group consisting of haplotypes 1-53 in Table 5; and

(b) a second nucleotide sequence which is complementary to the first nucleotide sequence.

2. The isolated polynucleotide of claim 1 which is a DNA molecule and comprises both the first and second nucleotide sequences and further comprises expression regulatory elements operably linked to the first nucleotide sequence.

3. A recombinant organism transformed or transfected with the isolated polynucleotide of claim 1, wherein the organism expresses an IL4R $\alpha$  protein encoded by the first nucleotide sequence.

4. The recombinant organism of claim 4 which is a nonhuman transgenic animal.

5. The isolated polynucleotide of claim 1, wherein the first nucleotide sequence is a polymorphic variant of a fragment of the IL4R $\alpha$  isogene, the fragment comprising one or more polymorphisms selected from the group consisting of: guanine at PS1, thymine at PS2, thymine at PS3, cytosine at PS4, thymine at PS6, adenine at PS7, cytosine at PS8, thymine at PS9, thymine at PS10, adenine at PS11, adenine at PS12, thymine at PS13, thymine at PS14, adenine at PS15, thymine at PS16, adenine at PS17, thymine at PS18, adenine at PS19, cytosine at PS20, cytosine at PS21, thymine at PS22, cytosine at PS23, thymine at PS25, thymine at PS27, cytosine at PS28, thymine at PS30, adenine at PS32, thymine at PS33, guanine at PS34, cytosine at PS35, cytosine at PS36, cytosine at PS37, thymine at PS38, guanine at PS39, guanine at PS40, adenine at PS41, thymine at PS44, and adenine at PS45.

6. An isolated polynucleotide comprising a nucleotide sequence which is a polymorphic variant of a reference sequence for the IL4R $\alpha$  cDNA or a fragment thereof, wherein the reference sequence comprises SEQ ID NO:2 and the polymorphic variant comprises adenine or guanine at a position corresponding to nucleotide 223, cytosine or thymine at a position corresponding to nucleotide 237, guanine or adenine at a position corresponding to nucleotide 244, thymine or cytosine at a position corresponding to nucleotide 291, cytosine or thymine at a position corresponding to nucleotide 501, guanine or adenine at a position corresponding to nucleotide 554, thymine or cytosine at a position corresponding to nucleotide 939, adenine or cytosine at a position corresponding to nucleotide 1198, guanine or thymine at a position corresponding to nucleotide 1242, thymine or cytosine at a position corresponding to nucleotide 1291, cytosine or thymine at a position corresponding to nucleotide 1293, thymine or cytosine at a position corresponding to nucleotide 1299, thymine or cytosine at a position corresponding to nucleotide 1507, cytosine or thymine at a position corresponding to nucleotide 1701, adenine or guanine at a position corresponding to nucleotide 1727, guanine or adenine at a position corresponding to nucleotide 1735, cytosine or thymine at a position

15

corresponding to nucleotide 2023, thymine or guanine at a position corresponding to nucleotide 2254 and thymine or cytosine at a position corresponding to nucleotide 2397.

7. A recombinant organism transformed or transfected with the isolated polynucleotide of claim 7, wherein the organism expresses a Interleukin 4 Receptor Alpha(IL4R $\alpha$ ) protein encoded by the polymorphic variant sequence.

8. The recombinant organism of claim 8 which is a nonhuman transgenic animal.

9. An isolated polypeptide comprising an amino acid sequence which is a polymorphic variant of a reference sequence for the IL4R $\alpha$  protein or a fragment thereof, wherein the reference sequence comprises SEQ ID NO: 3 and the polymorphic variant is encoded by an isogene defined by one of the haplotypes shown in Table 5.

10. An isolated antibody specific for and immunoreactive with the isolated polypeptide of claim 10.

11. A method for screening for drugs targeting the isolated polypeptide of claim 10 which comprises contacting the IL4R $\alpha$  polymorphic variant with a candidate agent and assaying for binding activity.

12. A composition comprising at least one genotyping oligonucleotide for detecting a polymorphism in the Interleukin 4 Receptor Alpha(IL4R $\alpha$ ) gene at a polymorphic site selected from PS1, PS2, PS3, PS4, PS6, PS7, PS8, PS9, PS10, PS11, PS12, PS13, PS14, PS15, PS16, PS17, PS18, PS19, PS20, PS21, PS22, PS23, PS25, PS27, PS28, PS30, PS32, PS33, PS34, PS35, PS36, PS37, PS38, PS39, PS40, PS41, PS44, and PS45.

13. The composition of claim 13, wherein the genotyping oligonucleotide is an allele-specific oligonucleotide that specifically hybridizes to an allele of the IL4R $\alpha$  gene at a region containing the polymorphic site.

14. The composition of claim 14, wherein the allele-specific oligonucleotide comprises a nucleotide sequence selected from the group consisting of of SEQ ID NOS:4-79, the complements of SEQ ID NOS: 4-79, and SEQ ID NOS:80-231.

15. The composition of claim 13, wherein the genotyping oligonucleotide is a primer-extension oligonucleotide.

16. A method for genotyping the Interleukin 4 Receptor Alpha(IL4R $\alpha$ ) gene of an individual, comprising determining for the two copies of the IL4R $\alpha$  gene present in the individual the identity of the nucleotide pair at each of PS1, PS2, PS3, PS4, PS6, PS7, PS8, PS9, PS10, PS11, PS12, PS13, PS14, PS15, PS16, PS17, PS18, PS19, PS20, PS21, PS22, PS23, PS25, PS27, PS28, PS30, PS32, PS33, PS34, PS35, PS36, PS37, PS38, PS39, PS40, PS41, PS44, and PS45.

17. The method of claim 17, wherein the determining step comprises:  
(a) isolating from the individual a nucleic acid mixture comprising both copies of the IL4R $\alpha$  gene, or a fragment thereof, that are present in the individual;

5

- (b) amplifying from the nucleic acid mixture a target region containing at least one of the polymorphic sites;
- (c) hybridizing a primer extension oligonucleotide to one allele of the amplified target region;
- (d) performing a nucleic acid template-dependent, primer extension reaction on the hybridized genotyping oligonucleotide in the presence of at least two different terminators of the reaction, wherein said terminators are complementary to the alternative nucleotides present at the polymorphic site; and
- (e) detecting the presence and identity of the terminator in the extended genotyping oligonucleotide.

10

18. A method for haplotyping the Interleukin 4 Receptor Alpha(IL4R $\alpha$ ) gene of an individual which comprises determining, for one copy of the IL4R $\alpha$  gene present in the individual, the identity of the nucleotide at each of PS1, PS2, PS3, PS4, PS6, PS7, PS8, PS9, PS10, PS11, PS12, PS13, PS14, PS15, PS16, PS17, PS18, PS19, PS20, PS21, PS22, PS23, PS25, PS27, PS28, PS30, PS32, PS33, PS34, PS35, PS36, PS37, PS38, PS39, PS40, PS41, PS44, and PS45.

19.

The method of claim 19, wherein the determining step comprises

- (a) isolating from the individual a nucleic acid molecule containing only one of the two copies of the IL4R $\alpha$  gene, or a fragment thereof that is present in the individual;
- (b) amplifying from the nucleic acid molecule a target region containing at least one of the polymorphic sites;
- (c) hybridizing a primer extension oligonucleotide to one allele of the amplified target region;
- (d) performing a nucleic acid template-dependent, primer extension reaction on the hybridized genotyping oligonucleotide in the presence of at least two different terminators of the reaction, wherein said terminators are complementary to the alternative nucleotides present at the polymorphic site; and
- (e) detecting the presence and identity of the terminator in the extended genotyping

5

10

oligonucleotide.

20.

A method for predicting a haplotype pair for the Interleukin 4 Receptor Alpha(IL4R $\alpha$ ) gene of an individual comprising:

- (a) identifying an IL4R $\alpha$  genotype for the individual at each of PS1, PS2, PS3, PS4, PS6, PS7, PS8, PS9, PS10, PS11, PS12, PS13, PS14, PS15, PS16, PS17, PS18, PS19, PS20, PS21, PS22, PS23, PS25, PS27, PS28, PS30, PS32, PS33, PS34, PS35, PS36, PS37, PS38, PS39, PS40, PS41, PS44, and PS45;
- (b) enumerating all possible haplotype pairs which are consistent with the genotype;
- (c) accessing data containing the IL4R $\alpha$  haplotype pairs determined in a reference population; and

5

- 21  
22. (d) assigning a haplotype pair to the individual that is consistent with the data.  
22. A method for identifying an association between a trait and at least one haplotype of the Interleukin 4 Receptor Alpha gene which comprises comparing the frequency of the haplotype in a population exhibiting the trait with the frequency of the haplotype in a reference population, wherein the haplotype is selected from haplotype numbers 1-53 shown in Table 5, wherein a higher frequency of the haplotype in the trait population than in the reference population indicates the trait is associated with the haplotype.

23  
24. The method of claim 22, wherein the trait is a clinical response to a drug targeting IL4R $\alpha$ .

25  
25. A computer system for storing and analyzing polymorphism data for the Interleukin 4 Receptor Alphagene, comprising:

- (a) a central processing unit (CPU);  
(b) a communication interface;  
(c) a display device;  
(d) an input device; and  
(e) a database containing the polymorphism data;

wherein the polymorphism data comprises the genotypes and haplotype pairs shown in Table 4 and the haplotypes shown in Table 5.

26  
26. A genome anthology for the Interleukin 4 Receptor Alpha(IL4R $\alpha$ ) gene which comprises IL4R $\alpha$  isogenes defined by haplotypes 1-53 shown in Table 5.

27  
27. A method for haplotyping the Interleukin 4 Receptor Alpha (IL4R $\alpha$ ) gene of an individual which comprises determining whether the individual has one or more haplotypes in Table 5.